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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,049	01/22/2004	Harriet L. Robinson	07917-217002	3662

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
01/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/763,049	ROBINSON ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7,11-14,20-22,32-35,38,42,43 and 57-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7,11-14,20-22,32-35,38,42,43 and 57-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/12/2009 has been entered.

Claim Status

Claims 1, 7, 32 and 38 are amended. Claims 4-6, 8-10, 15-19, 23-31, 36-37, 39-41, and 44-56 are canceled. Claims 59-60 are newly added. Claims 1-3, 7, 11-14, 20-22, 32-35, 38, 42-43, and 57-60 are under current examination.

Priority

This application claims benefit from as a CON of 08/187,879 filed on 01/27/1994 (US-PAT 6,841,381), which is a CIP of 08/009,833 filed on 01/27/1993 (US-PAT 5,643,578), which is a CIP of 07/855,562 filed 03/23/1992 (ABN). The instant application has been granted the benefit date, 23 March 1992, from the application 07/855,562.

RESPONSE TO ARGUMENTS

35 USC § 103

The rejection of claims 1-3, 7, 11-14, 20-22, 32-35, 38, 42-43 and 57-58 under 35 U.S.C. 103(a) as being unpatentable over Felgner et al. (WO90/11092) in view of Huylebroeck et al. (Gene. June 1988. 66(2): 163-81) and further in view of Townsend et al. (Cell. November 1984; 39(1):13-25) and further in view of Atkinson et al. (US-4,861,864, issued 29 Aug 1989) and further in view of Andrianov et al. (US-5,529,777, issued 25 June 1996) is withdrawn. The examiner has decided to simplify the obviousness rejection.

The applicant has noted that Adkinson and Andrianov references are no longer necessary for the rejection. These references were introduced to account for limitations directed to rotavirus antigens and alginate polymers, which have been cancelled from the pending claims. Although superfluous, these references were maintained in the obviousness rejection in the last Action. The examiner has decided to remove the Adkinson and Andrianov references from the Obviousness rejection. As this would result in a new grounds of rejection, the examiner has decided to withdraw the Obviousness rejection of the last action.

Therefore, the examiner hereby withdraws the rejection of claims 1-3, 7, 11-14, 20-22, 32-35, 38, 42-43 and 57-58 under 35 U.S.C. 103(a) as being unpatentable over Felgner et al. (WO90/11092) in view of Huylebroeck et al. (Gene. June 1988. 66(2): 163-81) and further in view of Townsend et al. (Cell. November 1984; 39(1):13-25) and

further in view of Atkinson et al. (US-4,861,864, issued 29 Aug 1989) and further in view of Andrianov et al. (US-5,529,777, issued 25 June 1996).

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 7, 11-14, 20-22, 32-35, 38, 42-43, and 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Felgner et al. (WO90/11092) in view of Huylebroeck et al. (Gene. June 1988. 66(2): 163-81) and further in view of Townsend et al. (Cell. November 1984; 39(1):13-25).

As the applicant has submitted arguments relevant to the new grounds of rejection, the examiner has addressed these remarks below.

Applicant's arguments (Remarks, pages 5-9) and claim amendments, filed 12 November 2009 regarding rejection of claims 1-3, 7, 11-14, 20-22, 32-35, 38, 42-43 and 57-58 under 35 USC 103 have been fully considered but they are unpersuasive.

The applicant has amended the pending claims narrowing the scope of the claims to a H1N1 antigen. New claims 59-60 particularly specify that the H1N1 antigen is type H1 hemagglutinin. Townsend teaches DNA mediated gene transfer of H1 hemagglutinin influenza antigen (abstract). Therefore, the cited art remains relevant over the amended and newly introduced claims.

The applicant has made several arguments.

The applicant has indicated that that he is dissatisfied with Felgner's statements regarding the protective effect of their nucleic acid vaccine. In particular, the applicant interprets Felgner's statements as being "merely prophetic...[and not] disclosing any actual supporting data" (Remarks, filed 11/12/2009, page 6, line 29, emphasis added by applicant). The examiner finds this argument unpersuasive because Felgner Example 9 describes actual data derived from administering a nucleic acid vaccine to mice followed by challenge with a live virus. Example 9 further demonstrates actual

supporting data for their conclusion that a protective effect has been generated. Particularly, Felgner assayed the number of infected cells (page 57, line 20-24) and the viral titer produced (page 57, lines 13-15) in these mice at 2, 4, and 8 weeks post injection, and demonstrated a 50% reduction of both viral titer and number of infected cells at 8 weeks. From this actual supporting data, Felgner concludes, "[t]ogether, these results indicate a moderate anti-viral effect of the (*in vivo*) treatment" (page 57, lines 24-25). Therefore, the examiner finds the applicant's arguments unpersuasive.

The applicant has argued that Felgner, Huylebroeck and Townsend do not teach provide teachings which support gene therapeutic methods of immunizing a vertebrate against H1N1 influenza virus infection. Contrary to the applicant's assertion, Townsend teaches DNA mediated gene transfer of H1 hemagglutinin influenza antigen (abstract).

The applicant suggests that the cited art does not provide a reasonable expectation of success. Contrary to the applicant's assertion, Felgner suggests a reasonably successful method of immunizing a vertebrate against virus infection by administering to said vertebrate prior to infection by said virus an plasmid DNA encoding a viral antigen, whereby a protective immune response comprising both a humoral immunity and a cell-protective immune response is elicited against the antigen to thereby protect the vertebrate against disease caused by a subsequent infection. Further, Townsend teaches DNA mediated gene transfer of H1 hemagglutinin influenza antigen (abstract). As Felgner has demonstrated the principle of prophylactic nucleic acid vaccination against a viral antigen, the examiner concludes a skilled artisan would deem the substitution of H1 hemagglutinin influenza antigen into the method of Felgner

as obvious and having a high likelihood of success. Accordingly, the examiner finds the applicant's argument unpersuasive.

Accordingly, the examiner finds the applicant's arguments unpersuasive and therefore, the arguments are insufficient to overcome the rejection below.

The rejection is elaborated below:

Claims 1-3, 7, 11-14, 20-22, 32-35, 38, 42-43 and 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Felgner et al. (WO90/11092) in view of Huylebroeck et al. (Gene. June 1988. 66(2): 163-81) and further in view of Townsend et al. (Cell. November 1984; 39(1):13-25).

Claims 1 and 16-17 are directed to methods of immunizing a vertebrate using a composition consisting essentially of a set of plasmid vectors in a physiologically acceptable medium, the plasmid vectors comprising DNA encoding an H1N1 influenza virus antigen operatively linked to a DNA promoter, which elicits a humoral and cell-mediated immune response against a H1N1 antigen. Claims 7 and 25-26 are directed to the further limitation that the virus is an influenza virus and the antigen is H1N1 hemagglutinin. Claim 32 is directed to using a gene gun to administer the compositions of the invention.

Felgner et al. teach plasmid vectors comprising "therapeutic polynucleotides… [which] code for immunity-conferring polypeptides, which act as endogenous immunogens to provoke a humoral or cellular response, or both" (page 17, lines 31-34). Felgner et al. suggest that tumor-specific antigens and viral protein antigens are appropriate for use in their invention (for example, page 4). Felgner et al. also teach

intradermal, intramuscular administration (page 11, lines 33-37) of naked polynucleotides in pharmaceutically acceptable carriers (page 8, line 24) to vaccinate a human (page 8, line 34). Furthermore, Felgner et al. teach "polynucleotides may be...delivered into muscle or skin using a vaccine gun" (page 36, lines 15-18). Felgner et al. also teach liposomal microsphere formulations of plasmid DNA and administration to the lung; the examiner believes this satisfies the limitations directed to pharmaceutically acceptable microsphere encapsulated plasmid vectors, in light of the teachings of the specification, described above. Claims 57-58 are directed to the methods of claim 1 and 32 respectively, wherein the promoter of the plasmid vectors comprises a cytomegalovirus promoter. Felgner et al. teach plasmid constructs having a viral coat protein gene operably linked to a cytomegalovirus (CMV) promoter (page 70, Example 19).

Felgner et al. do not teach specific antigens for influenza. Felgner et al. also do not specifically teach administration of set of plasmids encoding antigens, although they do teach co-transfection of two different plasmids to the cells.

Huylebroeck et al. teach plasmid DNA mediated gene transfer of two different influenza A antigens, including hemagglutinin (abstract). Huylebroeck et al. teach cotransfection of plasmids and co-expression of hemagglutinin A and influenza matrix protein M_1 in animal cells.

Townsend et al. teach plasmids comprising hemagglutinin antigens. Townsend teaches DNA mediated gene transfer of H1 hemagglutinin influenza antigen (abstract). Townsend et al. also teach “isolated full-length influenza gene clones is now routine”

(page 13, col.2). Furthermore, Townsend et al. teach, "there are implications for vaccine design…a vaccine that presents nucleoprotein in an appropriate form that could stimulate crossreactive CTL memory might be crossprotective between pandemic influenza A viruses" (page 22, col.2).

Huylebroeck et al. and Townsend et al. do not specifically teach DNA vaccines. These references also do not teach immunization using sets of plasmids encoding the antigens.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to immunize a vertebrate against an influenza virus or rotavirus by administering a composition consisting essentially of a set of plasmid vectors comprising DNA encoding either influenza virus antigens. Furthermore, it would have been obvious to use a gene gun to administer the DNA vaccines. In addition, it would have been obvious to use sets of plasmids to administer plasmids comprising antigens.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (plasmids comprising influenza or rotavirus antigens, methods of DNA vaccination, and gene gun administration) are taught by Felgner et al. or Huylebroeck et al. or Townsend et al. and further they are used as vaccines or are shown to be involved in inducing Cytotoxic T Lymphocyte responses and/or humoral

immune responses. It would be therefore predictably obvious to use a combination of these elements in a DNA vaccine. The methods of combining the elements with "sets of plasmids" are predictable; and therefore they are likewise obvious. Co-administration of plasmids has been performed in the art and is merely a variation of administration.

The cited art provides the skilled artisan with a reasonable expectation of success. Felgner suggests a reasonably successful method of immunizing a vertebrate against virus infection by administering to said vertebrate prior to infection by said virus a plasmid DNA encoding a viral antigen, whereby a protective immune response comprising both a humoral immunity and a cell-protective immune response is elicited against the antigen to thereby protect the vertebrate against disease caused by a subsequent infection. Further, Townsend teaches DNA mediated gene transfer of H1 hemagglutinin influenza antigen (abstract). As Felgner has demonstrated the principle of prophylactic nucleic acid vaccination against a viral antigen, the examiner concludes a skilled artisan would deem the substitution of H1 hemagglutinin influenza antigen into the method of Felgner as obvious and having a high likelihood of success.

Therefore the method as taught by Felgner et al. in view of Huylebroeck et al. and further in view of Townsend et al. would have been *prima facie* obvious over the method of the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7, 11, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Tite et al. (Immunology. 1990; 70:540-546).

Claim 1 is directed to a method of immunizing a vertebrate against an H1N1 influenza virus infection, said method comprising administering to a vertebrate, prior to infection by an H1N1 influenza virus, a composition consisting essentially of a set of plasmid vectors in a physiologically acceptable medium, the plasmid vectors comprising DNA encoding an H1N1 influenza virus antigen operatively linked to a DNA promoter, whereby a protective immune response comprising both a humoral and cell-mediated immune response against the antigen, to thereby protect the vertebrate against disease caused by a subsequence infection by an H1N1 influenza virus.

Tite et al. teach "A plasmid encoding the influenza nucleoprotein gene from A/NT/60/68 virus was transduced into the attenuated *Salmonella typhimurium* aroA-strain SL3261. The bacterial vector expressing the viral gene product was able to induce both humoral and cell-mediated immune responses to the nucleoprotein antigen." (Summary). Tite et al teach that "delivery of the NP molecule to the immune system using the live carrier SL3261 generated both systemic T- and B-cell immunity" (page 544, col.1, Oral administration, last sentence), thereby demonstrating a protective

immune response comprising both a humoral and cell-mediated immune response against the antigen. Tite et al. also teach that the virus used to challenge the vaccinated mice is strain of H1N1 influenza virus identified as A/Puerto Rico/8/34 (A/PR8) (page 541, col.1, Viruses).

Claim 7 is directed to the method of claim 1 wherein the antigen is an H1N1 influenza antigen. As the influenza nucleoprotein gene from A/NT/60/68 virus has been demonstrated as providing an antigen which generates a protective immune response against H1N1 influenza virus, the examiner is interpreting the influenza nucleoprotein gene from A/NT/60/68 virus antigen as being an H1N1 influenza antigen.

Claim 11 is directed to the method of claim 1, wherein the vertebrate is a mammal. Tite teaches vaccination of mice.

Claim 14 is directed to the method of claim 1, wherein the composition is administered to a vertebrate by contacting the composition to a mucosal surface of the vertebrate. Tite teaches administration of the composition to gastric mucosa.

Accordingly, the Tite et al. anticipated the instant claims

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 7, 11-14, 20-22, 32-35, 38, 42-43 and 57-60 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-13 and 22-28 of copending Application No. 11/178,588 (US2006/0014714). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of both the instant application and the co-pending application are directed to DNA vaccination using plasmids encoding a H1 hemmaglutinin influenza antigen, which induce both a humoral immune response and a cytotoxic immune response.

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,566,454.

Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of both the instant application and the issued patent are directed to DNA vaccination comprising administration of nucleic acids encoding a H1 hemmaglutinin influenza antigen, which induce both a humoral immune response and a cytotoxic immune response. Claim 1 of U.S. Patent No. 7,566,454 recites a H1 Hemmaglutinin influenza antigen which has been codon-optimized for expression in human cells. While the claimed invention could be used in veterinary medicine, it would also be considered for use in human medicine, therefore using a codon-optimized H1 hemmaglutinin influenza antigen would be an obvious modification of the instantly claimed method.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Scott Long/
Patent Examiner, Art Unit 1633